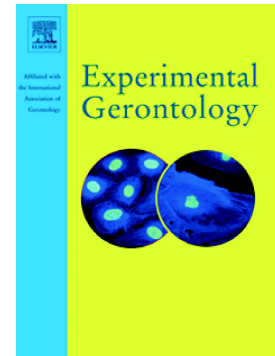


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Prospective Associations of Low Muscle Mass and Strength with Health-Related Quality of Life over 10-year in Community-dwelling Older Adults

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Abstract:

Aims: This study aims to describe the associations of low muscle mass, handgrip (HGS) and lower-limb muscle strength (LMS) with health-related quality of life (HRQoL) over 10 years in community-dwelling older adults.

Methods: Participants (N=1002; 51% women; mean age 63 ± 7.4 years) were prospectively followed for 10 years. HRQoL was measured using the validated assessment of quality of life (AQoL) instrument. Appendicular lean mass (ALM) was assessed using dual energy X-ray absorptiometry and normalised to body mass index (BMI). HGS and LMS were assessed using dynamometers. Low ALM/BMI (ALM/BMI_{LOW}), LMS (LMS_{LOW}) and HGS (HGS_{LOW}) at baseline were defined as the lowest 20% of the sex-specific distribution for each measure. Linear mixed effect regression models, adjusting for confounders, were used to estimate the association between ALM/BMI_{LOW} , LMS_{LOW} , and HGS_{LOW} at baseline and HRQoL over 10 years.

Results: Participants with LMS_{LOW} ($\beta = -0.061$, 95% CI: $-0.089, -0.033$) and women ($\beta = -0.089$, 95% CI: $-0.129, -0.049$) but not men ($\beta = -0.023$, 95% CI: $-0.064, 0.019$) with HGS_{LOW} had clinically meaningful reductions in HRQoL over 10 years compared to those with normal strength. There was a weaker but statistically significant association between ALM/BMI_{LOW} and 10-year HRQoL ($\beta = -0.038$, 95% CI: $-0.068, -0.008$).

Conclusions: Lower-limb muscle strength and handgrip strength (in women only), which can be easily measured in clinical practice, appear more important than muscle mass for HRQoL.

Keywords: Health-related quality of life, body composition, muscle mass, muscle strength

Introduction

Age-related decline in skeletal muscle mass and function is associated with health outcomes such as falls risk, fracture, poor mobility and physical disability that could impact older adults' independence and quality of life (Balogun et al. 2017; Hairi et al. 2010; Hirani et al. 2015). However, studies examining the relationship between muscle mass and function and health related quality of life (HRQoL) are sparse and largely cross-sectional (Woo et al. 2016). These studies showed that HRQoL, particularly the physical health domain, is lower among older people with low muscle mass and strength (Beaudart et al. 2015; Go et al. 2013; Manrique-Espinoza et al. 2017; Samuel et al. 2012; Sayer et al. 2006). However, it is unclear whether cross-sectional associations track over time.

While both muscle mass and strength decrease with age, the two processes do not occur at the same rate and may be the result of dissimilar pathophysiological processes (Clark and Manini 2008; Goodpaster et al. 2006; Rizzoli et al. 2013). Prior studies suggest that low muscle mass and strength may have different impacts on health outcomes in older people (Balogun et al. 2017; Hairi et al. 2010; Schaap et al. 2013). Despite these differences, few long-term prospective studies have compared the associations of low muscle mass and strength with HRQoL in community-dwelling older adults. Indeed, clarification of the relationship between low muscle mass and strength and HRQoL of older people may be important in the design of interventions to improve QoL. Therefore, this prospective study aims to describe the association of low muscle mass, handgrip and lower-limb muscle strength assessed at baseline with HRQoL over 10 years in community-dwelling older adults. We hypothesized that low muscle strength may be more closely related to HRQoL than muscle mass.

Data and Methods

Sample and Study Setting:

The Tasmanian Older Adult Cohort (TASOAC) study is a prospective, population-based study primarily aimed at examining the causes and progression of osteoarthritis. Participants aged 50 years and above were selected using a sex-stratified random sampling technique from the electoral roll in Southern Tasmania (population 229,000). A total of 1099 adults (response rate = 57%) consented to participate in the study. Participants were excluded if they had any implants that would prevent them from undergoing an MRI or they were living in a nursing home. Participants who consented to participate in the study were invited to attend a clinic at the Menzies Institute for Medical Research, Hobart, Tasmania between March 2002 and September, 2004. They were invited for follow-up clinic assessments at 2.5, 5, and 10 years after the initial clinic assessment. The study was approved by the Southern Tasmanian Health and Medical Research Ethics Committee and written informed consent was obtained from all participants.

Health-related quality of life over 10 years

HRQoL was assessed at baseline, 2.5, 5 and 10 years using the Assessment of Quality of life (AQoL-4D) questionnaire. The AQoL-4D is a validated generic questionnaire designed for the Australian population, however, it has been used in other populations including the United States, United Kingdom, Germany, India and Ireland (Hawthorne et al. 1999). AQoL was developed using state of the art psychometric properties and it is sensitive to varying health states (Hawthorne et al. 2001; Hawthorne et al. 1999). AQoL has been used in several studies to assess the QoL of individuals with varying health conditions including cardiovascular diseases, neurological disorders, mental health and musculoskeletal health (Anandacoomarasamy et al. 2009; Hill et al. 2015; Spinks et al. 2014; van Offen et al. 2017). Furthermore, the predicted utilities in AQoL are similar to those from the other generic utility instruments including EuroQol (EQ-5D) and the Canadian Health Utilities Index (HUI)

(Hawthorne et al. 2001). Compared to the 36-item short-form survey (SF-36), AQoL appears to be more suitable for evaluating HRQoL in epidemiologic studies involving older people, due to its robust psychometric properties (Osborne et al. 2003).

AQoL consists of 12 items covering four dimensions and each dimension has three items. The four dimensions and their corresponding items are: (1) independent living (self-care, activities of daily living), (2) physical senses (sight, hearing and communication), (3) social relationships (social isolation, relationship and family role) and (4) psychological wellbeing (sleep, anxiety and pain). The scores for items in each domain were transformed and summed to a life-death utility scale that ranges from 1.00 (full HRQoL) to 0.00 (death-equivalent health state) to -0.04 (health states worse than death) (Hawthorne and Osborne 2005; Richardson et al. 1998). The minimum important difference in AQoL score for the Australian population is 0.06 (Hawthorne and Osborne 2005). This score provides a measure of the smallest difference in AQoL score that is considered to be of a significant change in the health state of Australians (Hawthorne and Osborne 2005).

Assessments of low muscle mass and strength at baseline: Lower-limb muscle strength (LMS) was measured to the nearest kilogram simultaneously for both limbs using a dynamometer (TTM Muscular Meter, Tokyo, Japan). Two trials were recorded and the average of the two trials was taken as previously described (Scott et al. 2011). The intra-class correlation coefficients of the first and second trial for lower-limb muscle strength assessments was 0.95 (95% CI: 0.94 – 0.96). Hand grip strength (HGS) in pounds per square inch (psi) was measured using a pneumatic handheld bulb dynamometer (North Coast™ bulb dynamometer; adult 0-30 psi, model no. 70154). The mean of the right and left-hand grip strength was calculated for each participant. The intra-class correlation coefficients of the first and second trial for the hand grip strength measurements was 0.96 (95% CI: 0.92 – 0.97). Participants in the lowest 20% of the sex-specific distribution for LMS and HGS at

baseline were classified as having low LMS (LMS_{LOW}) and low HGS (HGS_{LOW}) (Hairi et al. 2010; Newman et al. 2003).

Body composition assessments at baseline: Whole and regional body composition of the participants were measured using dual energy X-ray absorptiometry (DXA; Hologic Delphi, Hologic, Waltham USA). Appendicular lean mass (ALM), in kilograms, was calculated as the sum of lean mass in the upper and lower limbs. Weight was measured to the nearest 0.1 kilogram using electronic scales (Heine, Dover, USA) with shoes and heavy clothing removed. Height was measured to the nearest 0.1 centimetre using Leicester stadiometer (Invicta, Leicester, UK), with shoes, socks and headgear removed. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. ALM was normalized to BMI as ALM-to-BMI ratio has been shown to be a potential criteria for identifying older adults with clinically relevant weakness (Cawthon et al. 2014). Participants in the lowest 20% of the sex-specific distribution for ALM/BMI at baseline were classified as having low muscle mass (ALM/BMI_{LOW}) (Hairi et al. 2010; Newman et al. 2003).

Potential confounders

Physical activity was measured over seven consecutive days using a pedometer (Omron HJ-003 & HJ-102; Omron Healthcare, Kyoto, Japan) as previously described (Scott et al. 2011). Age, sex, and medical history was recorded using a questionnaire. Presence of chronic conditions was assessed by responding yes or no to the question “Have you ever been diagnosed by a doctor as having any of the following?” The chronic conditions listed included: stroke, diabetes, rheumatoid arthritis, asthma, osteoporosis, cardiovascular disease (hypertension, thrombosis, bronchitis/emphysema, or heart attack). A score was then calculated as the total number of diagnosed chronic conditions.

Data analysis:

Means with standard deviations were used to summarize continuous variables, and percentages with participant numbers to describe categorical variables. Linear mixed effect regression analyses with adjustment for age at baseline, sex, self-reported pain and number of chronic conditions were used to estimate the association between low ALM/BMI, HGS and LMS assessed at baseline and AQL scores over 10 years. Statistical interaction between sex and each muscle parameter was assessed by a test of significance of a (sex \times muscle mass or function) product term. Data were analysed using Stata version 12.

Results

A total of 1002 participants with complete body composition, muscle strength and quality of life assessments at baseline were included in the analysis. Of these, 818 (82%), 722 (72%) and 539 (54%) respectively attended the 2.5, 5 and 10 years follow-up assessments.

Participants were lost to follow-up for reasons such as death, withdrawal of consent, institutionalization, moving interstate or overseas and having a joint replacement (see Supplementary Figure for more details). Participants lost to follow-up were older at baseline (64.5 ± 8.0 vs. 62.5 ± 7.3 , $P=0.001$), more commonly female (57% vs. 43% in men, $P=0.020$), had poorer baseline ALM (23.3 ± 5.3 kg vs. 24.7 ± 5.3 kg, $P<0.001$), HGS (11.3 ± 2.9 psi vs. 12.2 ± 3.1 psi, $P<0.001$) and LMS (82.6 ± 45.6 kg vs. 95.3 ± 49.7 kg, $P=0.001$) than those who completed the 10-year follow-up. No difference in baseline HRQoL ($P=0.323$) was observed between participants loss to follow-up (0.76 ± 0.19) and those retained in the study (0.77 ± 0.18). Table 1 shows the baseline characteristics of the participants stratified by low muscle mass and strength. Participants with ALM/BMI_{LOW}, HGS_{LOW} and LMS_{LOW} were older, shorter, had higher levels of knee and foot pain, lower levels of physical activity and greater number of chronic conditions compared to participants with normal muscle mass and

strength. Body weight was significantly lower in participants with low HGS and LMS whereas it was higher in those with ALM/BMI_{LOW}. Total body fat was significantly higher only in participants with ALM/BMI_{LOW}. Participants with ALM/BMI_{LOW} had higher hip pain and lower serum 25-hydroxyvitamin D compared to those with normal ALM/BMI, whereas no significant difference in hip pain and serum 25-hydroxyvitamin D was observed between participants with normal and low LMS or HGS. There were no statistical differences in sex and smoking status between participants with low and normal ALM/BMI, LMS and HGS. Figure 1 shows the mean predicted HRQoL scores (predictive margin) over time for participants with low and normal ALM/BMI, LMS and HGS. Participants with ALM/BMI_{LOW}, HGS_{LOW} and LMS_{LOW} consistently had a lower HRQoL over time compared to those with normal muscle mass and strength.

The associations between low muscle mass and strength at baseline and HRQoL over 10 years are shown in Table 2. Of note, the minimal important difference in the HRQoL score (overall health state utility) is 0.06 for the Australian population (Hawthorne and Osborne 2005).

ALM/BMI_{LOW} at baseline was associated with lower HRQoL over 10years ($\beta = -0.038$, 95% CI: $-0.068, -0.008$) with no evidence of an interaction between sex and ALM/BMI_{LOW} ($P = 0.680$). Furthermore, ALM/BMI_{LOW} was associated with a lower independent living ($\beta = -0.018$, 95% CI: $-0.032, -0.003$) and psychological wellbeing ($\beta = -0.026$, 95% CI: $-0.041, -0.011$) component of HRQoL but not with social relationship ($\beta = -0.012$, 95% CI: $-0.031, 0.007$) or physical senses components ($\beta = -0.004$, 95% CI: $-0.017, 0.009$) of HRQoL.

Participants with LMS_{LOW} at baseline had a clinically meaningful and significantly lower HRQoL over 10 years ($\beta = -0.061$, 95% CI: $-0.089, -0.033$). The association between LMS_{LOW} ($\beta = -0.059$, 95% CI: $-0.087, -0.032$) and HRQoL remained substantially lower

after further adjustment for ALM/BMI_{LOW} ($\beta = -0.035$, 95% CI: -0.064 , -0.006)

(Supplementary Table). There was no evidence for an interaction between sex and LMS_{LOW} ($P = 0.418$) for HRQoL. Furthermore, all four components of HRQoL were significantly lower in participants with LMS_{LOW}: independent living ($\beta = -0.024$, 95% CI: -0.038 , -0.010), social relationships ($\beta = -0.018$, 95% CI: -0.036 , -0.0003), physical senses ($\beta = -0.016$, 95% CI: -0.028 , -0.003) and psychological wellbeing ($\beta = -0.029$, 95% CI: -0.044 , -0.015).

The association between HGS_{LOW} at baseline and HRQoL over 10 years was modified by sex ($P = 0.008$), hence, the results are presented separately for men and women. For men, there was no significant relationship between HGS_{LOW} at baseline and HRQoL or any of the four components of HRQoL (all $P > 0.05$). However, among women, HGS_{LOW} at baseline was significantly associated with a clinically meaningful lower level of HRQoL over 10 years ($\beta = -0.089$, 95% CI: -0.129 , -0.049). Furthermore, women with HGS_{LOW} also had lower scores for the independent living ($\beta = -0.037$, 95% CI: -0.058 , -0.015), physical senses ($\beta = -0.021$, 95% CI: -0.037 , -0.005), psychological wellbeing ($\beta = -0.038$, 95% CI: -0.060 , -0.017) but not social relationships components of HRQoL ($\beta = -0.020$, 95% CI: -0.045 , 0.005). The association between baseline HGS_{LOW} ($\beta = -0.087$, 95% CI: -0.128 , -0.047) and HRQoL over 10 years remained significant after further adjustment for ALM/BMI_{LOW}, whereas the association with ALM/BMI_{LOW} was not ($\beta = -0.015$, 95% CI: -0.056 , 0.026) (Supplementary Table).

Discussion

This is the first long-term prospective study, to our knowledge, investigating the association between muscle mass, upper- and lower-limb muscle strength and HRQoL among community-dwelling older adults. Participants with LMS_{LOW} and women with HGS_{LOW} had a clinically meaningful and significantly lower HRQoL over 10 years compared to those with

normal strength. The association between ALM/BMI_{LOW} and HRQoL over 10 years was weaker and ALM/BMI_{LOW} did not affect the association between handgrip or lower-limb muscle strength and HRQoL. This demonstrates that muscle strength, which is closely related to physical performance and easy to measure in clinical practice, is a more important predictor of long-term quality of life in community-dwelling older adults than muscle mass.

In older adults, both men and women with lower muscle mass, lower-limb muscle strength and women but not men with lower handgrip strength at baseline had lower HRQoL over 10 years. Interestingly, a greater and more clinically meaningful difference (approaching or exceeding 0.06) in HRQoL (Hawthorne and Osborne 2005) was observed for older adults with LMS_{LOW} and women with HGS_{LOW} than in those with low muscle mass, the latter effect being around 40 – 60% the magnitude of the former two. One reason for this could be that age-associated loss of muscle strength occurs at a faster rate than loss of muscle mass (Goodpaster et al. 2006). A rapid loss of muscle strength can result in early onset of functional impairments, physical inactivity and poor social engagement that could have a larger impact on HRQoL. Contrary to our findings, a recent 3-year prospective study suggested that muscle mass, not muscle strength, was significantly associated HRQoL (Trombetti et al. 2016). However, this study was limited by its very small sample size (n=26) and because QoL was assessed using only the physical components of SF-36 rather than the combined physical and mental components. Indeed, physical components of SF-36 correlates poorly with muscle strength and this measure alone may not be a suitable outcome measure in musculoskeletal studies (Samuel et al. 2012). Consistent with our findings, several studies have documented the clinical utility of muscle strength as a better predictor of health and HRQoL in older adults (Cawthon et al. 2009; Samuel et al. 2012). This, combined with the fact that low muscle mass did not affect the clinically meaningful decrease in HRQoL in individuals with low muscle strength, suggest that muscle strength may be more important

than muscle mass for HRQoL. Women with HGS_{LOW} had a lower HRQoL over 10 years, while no significant association was found in men. The reason for this observation is unclear, nonetheless, this finding is consistent with prior studies which suggest that maintenance of HGS appears to be more important in reducing detrimental health outcomes in women compared to men (Arvandi et al. 2016). One possible explanation is that women generally have a lower upper-limb muscle strength than men. For instance, in our sample, mean (SD) baseline HGS for women was 10.0 (1.9) psi compared to 14.1 (2.6) psi in men. Hence, any loss of upper-limb strength in women is more likely to result in difficulty performing tasks required to maintain function (Janssen et al. 2000). Potentially this contributes to an increased likelihood of loss of independence and poorer HRQoL in women.

Participants with ALM/BMI_{LOW}, LMS_{LOW}, and women with HGS_{LOW} had lower scores on the independent living component of HRQoL. This demonstrates the importance of preserving muscle mass and strength in order to perform tasks associated with maintaining independent living over a decade. A requirement for independent living in old age is the ability to perform (instrumental) activities of daily living (ADL/IADL) with no difficulty (Tanimoto et al. 2012). In several studies, older adults with advanced muscle loss have had a reduced capacity to perform ADLs as well as an increased need for health support services and subsequent institutionalisation (Hairi et al. 2010; Hirani et al. 2015; Tanimoto et al. 2012). Public health initiatives that help older adults maintain muscle mass and strength will be important to decrease dependency in later life.

Social relationship component of HRQoL was significantly lower only in individuals with LMS_{LOW}, suggesting that lower extremity muscle strength could be important in maintaining an interpersonal relationship with friends and family over the long-term. Contrary to our findings in this community-dwelling population, previous cross-sectional studies among pre-frail and frail older adults have reported no significant association between muscle strength

and social participation (Haider et al. 2016; Warren et al. 2016). It may be that poor lower extremity muscle strength in independent living older adults could result in greater social isolation than in frailer adults with complex medical conditions and are likely to receive to health supports. This could occur via impairment in mobility, as a reduction in mobility is associated with a decline in physical function (Satariano et al. 2012). Interestingly, physical senses domain of HRQoL was lower in older adults with LMS_{LOW} and women with HGS_{LOW} whereas no associations was observed for ALM/BMI_{LOW} . Low muscle strength is not likely to be a direct cause of poorer physical senses, rather it could lead to the development of some chronic diseases which affect physical senses. Furthermore, low muscle strength may also be a marker of pre-existing or current chronic conditions (such as diabetes) affecting physical senses like visual function.

Interestingly, the psychological wellbeing component of HRQoL was lower in older adults with ALM/BMI_{LOW} , LMS_{LOW} , and women with HGS_{LOW} . This is consistent with prior studies reporting poorer psychological health in older adults with low muscle mass and strength, although the mechanism underlying the association between age-related muscle loss and psychological wellbeing is not entirely clear (Alfaro-Acha et al. 2006; Chang et al. 2017; Hsu et al. 2014; Manrique-Espinoza et al. 2017; Taekema et al. 2010). Potentially loss of independent living skills associated with low muscle mass and strength could have physical and emotional impacts on older adults, and could contribute to poorer psychological wellbeing. For instance, a recent systematic review and meta-analysis of 15 observational studies reported a significantly higher odds of depression in older adults with sarcopenia (Chang et al. 2017). Muscle function may be related to psychological wellbeing because they both have a central nervous system involvement and muscle weakness may be an early indicator of age-related decline in central nervous system that is manifested in poor mental health (Alfaro-Acha et al. 2006). Indeed, resistance exercises have been shown to lead to an

improvement of, and prevention of decline in mental health, in addition to improvement in muscle strength suggesting a link between the two processes (Chang et al. 2012; Katula et al. 2008). Further clinical studies incorporating brain morphology and neuroplasticity are warranted to determine the physiological mechanisms through which low muscle mass and strength may be related to poorer psychological wellbeing (Mavros et al. 2016).

The strengths of this study includes the 10-year follow-up period and the use of a population-based sample which increases its generalizability. In addition, muscle mass was assessed using DXA, a valid and accurate tool for assessing muscle mass. However, this study has a number of limitations. Forty-six percent of the participants were lost to follow-up over 10 years. Such missing data is not unexpected in a long-term prospective study involving older people. The participants lost to follow-up were older at baseline and they had poorer baseline ALM, weaker HGS and LMS than those who completed the 10-year follow-up. Therefore, the loss to follow-up could lead to an underestimation of the relationship between low muscle mass/strength and HRQoL. Nevertheless, the missing data were accommodated in the linear mixed effect models by using maximum likelihood estimation which estimates means and intercept based on all available data. This minimize bias and increase power as participants with missing follow-up data were retained in the analysis. Furthermore, handgrip strength was measured using a pneumatic bulb dynamometer rather than hydraulic dynamometer (e.g. Jamar), hence the strength cut-points indicating poorer HRQoL observed in this study may be different for assessments derived from hydraulic dynamometers.

However, previous studies have found high concordance between the two methods (Ward and Adams 2007). HRQoL was assessed using a generic questionnaire rather than a disease-specific HRQoL measure such as the sarcopenia and quality of Life (SARQoL) questionnaire. Unlike SARQoL, AQoL was not originally designed to assess the impact of age-related loss of muscle mass and function, nonetheless, some of the items (for instance,

difficulty with ADL, mobility and pain) assessed in SarQoL are also captured in AQoL. AQoL is a commonly used tool specifically designed for the Australian population demonstrating both validity and reproducibility (Hawthorne and Osborne 2005). Lastly, our measure of chronic conditions as a potential confounder was a crude measure that did not take into account disease severity. These simple questions have been validated for a number of diseases and our approach of counting the number of chronic conditions has been used in operational definitions of multi-morbidity (Fortin et al. 2017; Hussain et al. 2015).

In conclusion, lower-limb muscle strength and handgrip strength (in women only) were a better predictor of HRQoL over 10 years compared to muscle mass. In this respect, measuring muscle strength in clinical practice appears to be a promising approach to identify older adults who are at risk of having a considerable decline in HRQoL as they age. As age-related decline in muscle strength is amenable to interventions, resistance exercise training aimed at improving muscle strength may have a beneficial impact on long term HRQoL.

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References:

- Alfaro-Acha A, Al Snih S, Raji MA, Kuo Y-F, Markides KS, Ottenbacher KJ (2006)
Handgrip strength and cognitive decline in older Mexican Americans *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 61:859-865
- Anandacoomarasamy A, Caterson ID, Leibman S, Smith GS, Sambrook PN, Fransen M, March LM (2009) Influence of BMI on health-related quality of life: Comparison between an obese adult cohort and age-matched population norms *Obesity* 17:2114-2118
- Arvandi M et al. (2016) Gender differences in the association between grip strength and mortality in older adults: results from the KORA-age study *BMC Geriatrics* 16:1-8
- Balogun S, Winzenberg T, Wills K, Scott D, Jones G, Aitken D, Callisaya M (2017)
Prospective Associations of Low Muscle Mass and Function with 10-year Falls Risk, Incident Fracture and Mortality in Community-dwelling Older Adults *Journal of Nutrition Health & Aging* 21:843–848 doi:10.1007/s12603-016-0843-6
- Beaudart C et al. (2015) Quality of life and physical components linked to sarcopenia: The SarcoPhAge study *Experimental gerontology* 69:103-110
doi:10.1016/j.exger.2015.05.003
- Cawthon PM et al. (2009) Do muscle mass, muscle density, strength, and physical function similarly influence risk of hospitalization in older adults? *Journal of the American Geriatrics Society* 57:1411-1419

- Cawthon PM et al. (2014) Cutpoints for low appendicular lean mass that identify older adults with clinically significant weakness The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 69:567-575
- Chang K-V, Hsu T-H, Wu W-T, Huang K-C, Han D-S (2017) Is sarcopenia associated with depression? A systematic review and meta-analysis of observational studies Age and Ageing:1-9
- Chang Y-K, Pan C-Y, Chen F-T, Tsai C-L, Huang C-C (2012) Effect of resistance-exercise training on cognitive function in healthy older adults: a review Journal of Aging and Physical Activity 20:497-517
- Clark BC, Manini TM (2008) Sarcopenia≠ dynapenia The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 63:829-834
- Fortin M, Almirall J, Nicholson K (2017) Development of a research tool to document self-reported chronic conditions in primary care Journal of Comorbidity 7:117-123
- Go SW, Cha YH, Lee JA, Park HS (2013) Association between sarcopenia, bone density, and health-related quality of life in Korean men Korean Journal of Family Medicine 34:281-288
- Goodpaster BH et al. (2006) The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 61:1059-1064

Haider S, Luger E, Kapan A, Titze S, Lackinger C, Schindler KE, Dorner TE (2016)

Associations between daily physical activity, handgrip strength, muscle mass, physical performance and quality of life in prefrail and frail community-dwelling older adults *Quality of Life Research* 25:3129-3138

Hairi NN et al. (2010) Loss of muscle strength, mass (sarcopenia), and quality (specific

force) and its relationship with functional limitation and physical disability: the Concord Health and Ageing in Men Project *Journal of the American Geriatrics Society* 58:2055-2062

Hawthorne G, Osborne R (2005) Population norms and meaningful differences for the

Assessment of Quality of Life (AQoL) measure Australian and New Zealand *journal of public health* 29:136-142

Hawthorne G, Richardson J, Day NA (2001) A comparison of the Assessment of Quality of

Life (AQoL) with four other generic utility instruments *Annals of medicine* 33:358-370

Hawthorne G, Richardson J, Osborne R (1999) The Assessment of Quality of Life (AQoL)

instrument: a psychometric measure of health-related quality of life *Quality of Life Research* 8:209-224

Hill CL et al. (2015) Fish oil in knee osteoarthritis: a randomised clinical trial of low dose

versus high dose *Annals of the rheumatic diseases:annrheumdis-2014-207169*

- Hirani V et al. (2015) Sarcopenia is associated with incident disability, institutionalization, and mortality in community-dwelling older men: the Concord Health and Ageing in Men Project Journal of the American Medical Directors Association 16:607-613
- Hsu YH, Liang CK, Chou MY, Liao MC, Lin YT, Chen LK, Lo YK (2014) Association of cognitive impairment, depressive symptoms and sarcopenia among healthy older men in the veterans retirement community in southern Taiwan: A cross-sectional study Geriatrics and Gerontology International 14:102-108
- Hussain MA, Huxley RR, Al Mamun A (2015) Multimorbidity prevalence and pattern in Indonesian adults: an exploratory study using national survey data BMJ open 5:e009810
- Janssen I, Heymsfield SB, Wang Z, Ross R (2000) Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr Journal of Applied Physiology 89:81-88
- Katula JA, Rejeski WJ, Marsh AP (2008) Enhancing quality of life in older adults: A comparison of muscular strength and power training Health and quality of life outcomes 6:1-8 doi:10.1186/1477-7525-6-45
- Manrique-Espinoza B, Salinas-Rodríguez A, Rosas-Carrasco O, Gutiérrez-Robledo LM, Avila-Funes JA (2017) Sarcopenia Is Associated With Physical and Mental Components of Health-Related Quality of Life in Older Adults Journal of the American Medical Directors Association

Mavros Y et al. (2016) Mediation of Cognitive Function Improvements by Strength Gains

After Resistance Training in Older Adults with Mild Cognitive Impairment:

Outcomes of the Study of Mental and Resistance Training Journal of the American Geriatrics Society 65:550-559

Newman AB et al. (2003) Sarcopenia: alternative definitions and associations with lower

extremity function Journal of the American Geriatrics Society 51:1602-1609

Osborne RH, Hawthorne G, Lew EA, Gray LC (2003) Quality of life assessment in the

community-dwelling elderly: validation of the Assessment of Quality of Life (AQoL)

Instrument and comparison with the SF-36 Journal of clinical epidemiology 56:138-147

Richardson J, Hawthorne G, Day N, Osborne R, McNeil H (1998) Difficulty with Life and

Death: Methodological Issues and Results from the Utility Scaling of the Assessment

of Quality of Life (AQoL) Instrument. Centre for Health Program Evaluation,

Melbourne:29 pages

Rizzoli R et al. (2013) Quality of Life in Sarcopenia and Frailty Calcified Tissue

International 93:101-120 doi:10.1007/s00223-013-9758-y

Samuel D, Rowe P, Hood V, Nicol A (2012) The relationships between muscle strength,

biomechanical functional moments and health-related quality of life in non-elite older

adults Age and Ageing 41:224-230 doi:10.1093/ageing/afr156

Satariano WA, Guralnik JM, Jackson RJ, Marottoli RA, Phelan EA, Prohaska TR (2012)

Mobility and Aging : New Directions for Public Health Action American Journal of
Public Health 102:1508-1516 doi:10.2105/AJPH.2011.300631

Sayer AA, Syddall HE, Martin HJ, Dennison EM, Roberts HC, Cooper C (2006) Is grip
strength associated with health-related quality of life? - Findings from the

Hertfordshire Cohort Study Age and Ageing 35:409-415 doi:10.1093/ageing/afl024

Schaap LA, Koster A, Visser M (2013) Adiposity, muscle mass, and muscle strength in
relation to functional decline in older persons Epidemiologic Reviews 35:51-65

Scott D, Blizzard L, Fell J, Jones G (2011) Prospective associations between ambulatory
activity, body composition and muscle function in older adults Scandinavian Journal
of Medicine & Science in Sports 21:e168-e175

Spinks J, Johnston D, Hollingsworth B (2014) Complementary and alternative medicine
(CAM) use and quality of life in people with type 2 diabetes and/or cardiovascular
disease Complementary therapies in medicine 22:107-115

Taekema DG, Gussekloo J, Maier AB, Westendorp RG, de Craen AJ (2010) Handgrip
strength as a predictor of functional, psychological and social health. A prospective
population-based study among the oldest old Age and ageing 39:331-337

Tanimoto Y et al. (2012) Association between muscle mass and disability in performing
instrumental activities of daily living (IADL) in community-dwelling elderly in Japan
Archives of gerontology and geriatrics 54:e230-e233

Trombetti A, Reid KF, Hars M, Herrmann FR, Pasha E, Phillips EM, Fielding RA (2016)

Age-associated declines in muscle mass, strength, power, and physical performance:

impact on fear of falling and quality of life *Osteoporosis International* 27:463-471

doi:10.1007/s00198-015-3236-5

van Offen M, van Rijen PC, Leijten FS (2017) Central lobe epilepsy surgery—(functional)

results and how to evaluate them *Epilepsy Research* 130:37-46

Ward C, Adams J (2007) Comparative study of the test-re-test reliability of four instruments

to measure grip strength in a healthy population *The British Journal of Hand Therapy*

12:48-54

Warren M, Ganley KJ, Pohl PS (2016) The association between social participation and

lower extremity muscle strength, balance, and gait speed in US adults *Preventive*

Medicine Reports 4:142-147

Woo T, Yu S, Visvanathan R (2016) Systematic Literature Review on the Relationship

Between Biomarkers of Sarcopenia and Quality of Life in Older People *The Journal*

of Frailty & Aging 5:88-99

Table 1: Baseline characteristics of the participants stratified by ALM/BMI, lower-limb muscle strength, and handgrip strength categories (N=1002)

Variables	ALM/BMI, kg/kg/m ²		Lower-limb muscle strength, kg		Handgrip strength, psi	
	Normal (N=816)	Low (N=186)	Normal (N=803)	Low (N=199)	Normal (N=802)	Low (N=200)
Age (years)	62.3±7.3	65.3±7.7	62.1±7.2	65.6±7.8	61.6±6.9	67.6±7.7
Female n (%)	416(51%)	95(52%)	407(51%)	104(52%)	409(51%)	102 (51%)
Weight (kilogram)	76.0±14.0	84.8±14.6	78.3±14.8	74.9±12.9	78.2±14.7	75.4±13.4
Height (centimetre)	168.2±8.6	162.1±8.8	167.6±9.0	165.0±8.6	167.5±8.9	165.3±9.0
Total body fat (kilogram)	26.5±7.7	34.9±9.1	28.1±8.7	28.2±8.7	28.0±8.7	28.4±8.6
Energy intake (Kilo Joules/day)	7784.4±2870.1	7269.3±2681.8	7769.8±2794.4	7361.4±3010.5	7754.2±2594.1	7721.6±2770.6
Physical activity (steps/day)	9087.3±3301.6	7043.1±3177.0	8915.3±3329.5	7870.8±3423.0	8941.9±3366.5	7769.3±3237.7
Smoking n (% yes)	404 (50%)	99 (53%)	405(51%)	98(49%)	411(51%)	92(46%)
Serum 25(OH)D (nmol/L)	54.1±18.7	47.2±16.9	53.0±18.4	52.1±19.1	52.9±18.7	52.5±18.0
Hip pain (%)	311(38%)	89(48%)	315(40%)	85(43%)	313(39%)	87(44%)
Knee pain (%)	344(43%)	102(55%)	337(42%)	109(55%)	338(43%)	108(54%)
Foot pain (%)	278(34%)	92(49%)	271(34%)	99(50%)	275(35%)	95(48%)
Number of chronic condition	1.3±1.3	2.0±1.6	1.3±1.2	1.9±1.6	1.3±1.3	1.8±1.5

Data are expressed as mean ± standard deviation unless otherwise indicated;

ALM/BMI: Appendicular lean mass/body mass index; 25(OH)D: 25-hydroxy vitamin D₃; psi: pounds per square inch. To convert psi to kilograms (kg) per centimetre squared multiply by 0.07031.

Table 2: Associations between baseline ALM/BMI, HGS, LMS status and health-related quality of life (HRQoL) over 10 years (N=818)

	HRQoL score	Component dimensions of HRQoL			
	(Overall health state utility)	Independent living	Social relationships	Physical senses	Psychological wellbeing
ALM/BMI _{LOW}	-0.038(-0.068, -0.008)	-0.018(-0.032, -0.003)	-0.012(-0.031, 0.007)	-0.004(-0.017, 0.009)	-0.026(-0.041, -0.011)
LMS _{LOW}	-0.061(-0.089, -0.033)	-0.024(-0.038, -0.010)	-0.018(-0.036, -0.0003)	-0.016(-0.028, -0.003)	-0.029(-0.044, -0.015)
HGS _{LOW} (Men)*	-0.023(-0.064, 0.019)	-0.009(-0.027, 0.009)	-0.021(-0.049, 0.007)	-0.007(-0.028, 0.013)	-0.006(-0.026, 0.014)
HGS _{LOW} (Women)*	-0.089(-0.129, -0.049)	-0.037(-0.058, -0.015)	-0.020(-0.045, 0.005)	-0.021(-0.037, -0.005)	-0.038(-0.060, -0.017)

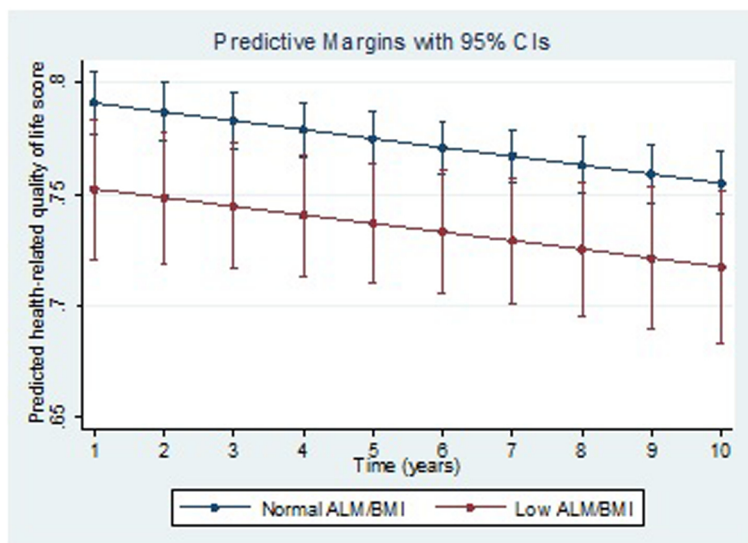
Negative scores indicate poorer health. *Sex interaction existed for HGS, therefore, the results is presented separately for men and women.

Analyses are adjusted for age, sex, physical activity, time to follow-up and number of chronic conditions. Data in bold indicates $P < 0.05$.

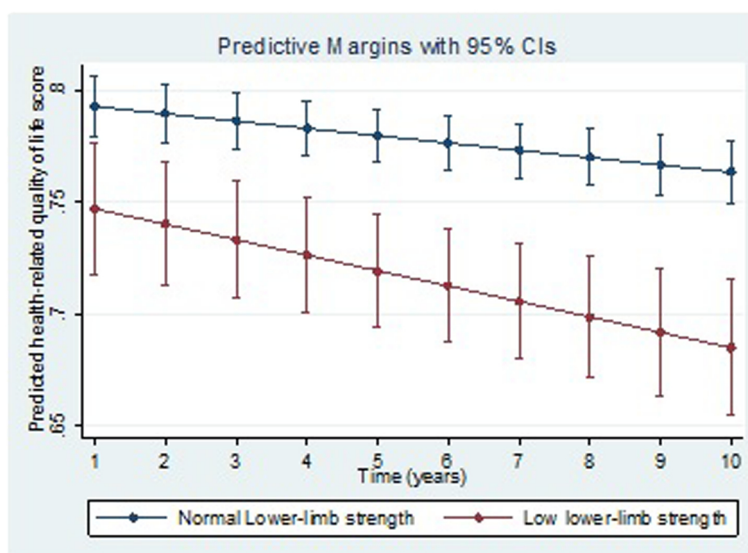
Note: The HRQoL score ranges from 1.00 (full HRQoL) to 0.00 (death-equivalent health state) to -0.04 (health states worse than death). The minimal important difference in HRQoL score (overall health state utility) for the Australian population is 0.06 [16].

ALM/BMI_{LOW}: Sex specific lowest 20% of appendicular lean mass (ALM)/body mass index [BMI] (kg/ kg/m²); **LMS_{LOW}**: Sex specific lowest 20% of lower-limb muscle strength (kg); **HGS_{LOW}**: Sex specific lowest 20% of handgrip strength (psi)

A



B



C

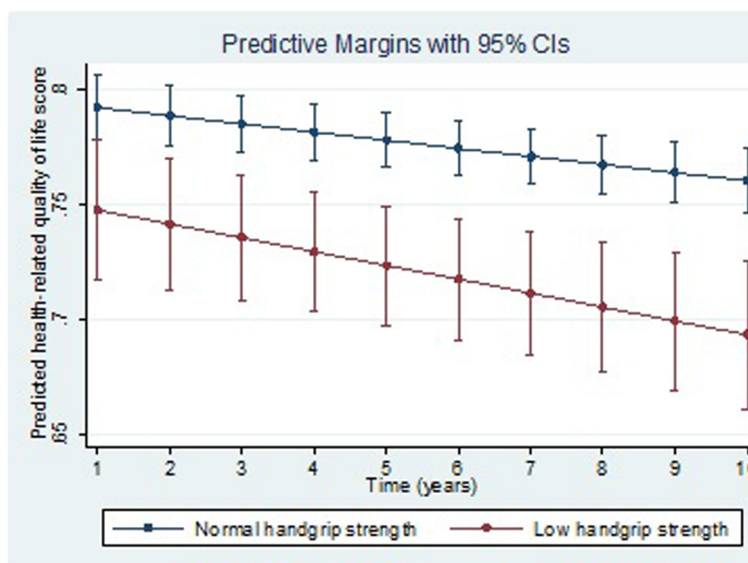


Figure 1